

-continued

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26

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23

The invention claimed is:

1. A double-stranded siRNA molecule against a target nucleic acid, wherein the double-stranded siRNA molecule comprises a first strand and a second strand,

wherein the first strand comprises a first stretch that is complementary to the target nucleic acid,

wherein the second strand comprises a second stretch that is complementary to the first stretch,

wherein the first strand and the second strand form a double-stranded structure comprising the first stretch and the second stretch,

wherein the double-stranded siRNA molecule is blunt ended on at least one end, and

wherein each stretch consists of at least 15 and fewer than 30 ribonucleotides and wherein the first stretch and the second stretch each comprises contiguous alternating modified ribonucleotides, wherein the alternating modified ribonucleotides alternate with unmodified or differently modified ribonucleotides.

2. The double-stranded siRNA molecule of claim 1, wherein the double-stranded siRNA molecule is blunt ended on the end defined by the 5' end of the first strand and the 3' end of the second strand.

3. The double-stranded siRNA molecule of claim 1, wherein the double-stranded siRNA molecule is blunt ended on the end defined by the 3' end of the first strand and the 5' end of the second strand.

4. The double-stranded siRNA molecule of claim 1, wherein the double-stranded siRNA molecule is blunt ended on both ends.

5. The double-stranded siRNA molecule of claim 1, wherein each of the first strand and the second strand consists of 17 to 30 ribonucleotides.

6. The double-stranded siRNA molecule of claim 1, wherein the first stretch and the second stretch are of the same length.

7. The double-stranded siRNA molecule of claim 1, wherein each of the first strand and the second strand is 17 to 23 nucleotides long.

8. The double-stranded siRNA molecule of claim 1, wherein each of the first strand and the second strand is 19 nucleotides long.

9. The double-stranded siRNA molecule of claim 1, wherein each of the first strand and the second strand is 21 nucleotides long.

10. The double-stranded siRNA molecule of claim 1, wherein each of the first strand and the second strand is 23 nucleotides long.

11. The double-stranded siRNA molecule of claim 1, wherein the modified ribonucleotides are selected from the group consisting of 2'-O-alkyl ribonucleotides, 2'-fluoro ribonucleotides and 2'-amino ribonucleotides.

12. The double-stranded siRNA molecule of claim 11, wherein the 2'-O-alkyl ribonucleotides are selected from the group consisting of 2'-O-methyl ribonucleotides and 2'-O-ethyl ribonucleotides.

13. The double-stranded siRNA molecule of claim 1, wherein the modified ribonucleotides are 2'-O-methyl ribonucleotides.

14. The double-stranded siRNA molecule of claim 13, wherein the 2'-O-methyl ribonucleotides alternate with the unmodified ribonucleotides.

15. The double-stranded siRNA molecule of claim 13, wherein the 2'-O-methyl ribonucleotides alternate with the differently modified ribonucleotides.

16. The double-stranded siRNA molecule of claim 15, wherein the differently modified ribonucleotides are 2'-fluoro ribonucleotides.

17. The double-stranded siRNA molecule of claim 1, wherein the alternating modified ribonucleotides of the first strand are shifted by at least one ribonucleotide relative to the unmodified or differently modified ribonucleotides of the second strand.

18. The double-stranded siRNA molecule of claim 1, wherein the first stretch and the second stretch each comprises contiguous alternating single 2'-O-alkyl modified ribonucleotides, and wherein the single 2'-O-alkyl modified ribonucleotides alternate with the unmodified ribonucleotides.

19. The double-stranded siRNA molecule of claim 18, wherein the single 2'-O-alkyl modified ribonucleotides of the first strand are shifted by one ribonucleotide relative to the single 2'-O-alkyl modified ribonucleotides of the second strand.